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10/089,450

03/29/2002

Gilbert Gorr

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EXAMINER

KUBELIK, ANNE R

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/089,450 | Applicant(s) GORR ET AL. | |
| | Examiner Anne R. Kubelik | Art Unit 1638 | |

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 December 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 17 and 19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 17 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-6, 17 and 19 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The rejection of claims 4-6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention is withdrawn in light of Applicant's amendment of the claims.

Claim Rejections - 35 USC § 112

4. Claims 1-6 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the production of secreted proteins in *Physcomitrella patens* by transformation with constructs that encode signal peptides operably linked to the proteins, does not reasonably provide enablement for a method for the production of secreted proteins in other mosses or in liverworts or a method for the production of proteins in *Physcomitrella patens* by transformation with constructs that do not encode signal peptides operably linked to the proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 7 June 2005, as applied to claims 1-6 and 17. Applicant's arguments and the Declaration of Dr. Gorr, both filed 7 December 2005 have been fully considered but they are not persuasive.

The claims are broadly drawn to a method for the production of proteins in mosses and liverworts, including *Physcomitrella*, *Funaria*, *Sphagnum*, *Ceratodon*, *Marchantia* and *Sphaerocarpos*.

The instant specification, however, only provides guidance for transformation of *P. patens* with a vector encoding vascular endothelial growth factor (VEGF) operably linked to a human ER transit peptide (pg 14-27).

The instant specification fails to provide guidance for transformation of other mosses or of liverworts. The specification fails to provide guidance for a method for the production of secreted proteins from a moss or liverwort when the protein is not produced with a signal peptide.

Baur et al (2005, J. Biotechnol. 119:332-342) teach that *P. patens* transformed with constructs encoding VEGF not operably linked to a transit peptide do not secrete any VEGF and produce very little intracellularly (Fig 2).

As the specification does not describe the transformation of any moss or liverwort other than *P. patens* with a heterologous gene, undue trial and error experimentation would be required to develop a transformation method for the other mosses and the liverwort as encompassed by the claims, if transformation is even obtainable.

Given the claim breadth and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that the emphasis in the enablement rejection is wrong, as the instant invention is a method of obtaining heterologous proteins from cultured transformed protonema tissue (response pg 7-8).

This is not found persuasive because transformation of mosses and liverworts within the full scope of the claims is required to obtain heterologous proteins from cultured transformed protonema tissue.

Applicant urges that other references cited in the prior Office action teach transformation of *C. purpureus* and *M. polymorpha* (response pg 8).

This is not found persuasive because neither the specification nor the prior art teach methods of transformation for any *Funaria*, *Sphagnum* or *Sphaerocarpos* species or for any *Physcomitrella*, *Ceratodon* or *Marchantia* species other than *P. patens*, *C. purpureus* or *M. polymorpha*, much less any protonema-forming moss or liverwort. There are, for example, at least 6 *Marchantia* species other than *M. polymorpha* (*M. calcarata*, *M. emarginata*, *M. foliacea*, *M. inflexa*, *M. paleacea*, and *M. subintegra*), and at least 161 *Sphagnum* species (including *S. acutirameum*, *S. affine*, *S. africanum*, *S. alegrense*, *S. amoenoides*, *S. andersonianum*, *S. angermanicum*, *S. angustifolium*, *S. annulatum*, *S. aongstroemii*, *S. arcticum*, *S. aureum*, *S. auriculatum*, *S. austinii*, *S. austro-americanum*, *S. azuayense*, *S. balticum*, *S. bartlettianum*, *S. billbuckii*, *S. bocainense*, *S. boliviae*, *S. bordasii*, *S. boyacanum*, *S. brachycaulon*, *S. brasiliense*, *S. brevirameum*, *S. buckianum*, *S. calymmatophyllum*, *S. capense*, *S. capillifolium*, *S. carolinianum*, *S. centrale*, *S. compactum*, *S. contortum*, *S. crispum*, *S. cristatum*, *S. crumii*, *S. cuculliforme*, *S. curvatulum*, *S. cuspidatulum*, *S. cuspidatum*, *S. cyclophyllum*, *S. cymbifolioides*, *S. davidii*, *S. denticulatum*, *S. ecuadorensense*, *S. ehyalinum*, *S. exquisitum*, *S. falciculatum*, *S. fallax*, *S. fimbriatum*, *S. fitzgeraldii*, *S. flaccidum*, *S. flavicomans*, *S. flexuosum*, *S. fuscum*, *S. geraisense*, *S. girgensohnii*, *S. gracilescens*, *S. guwassanense*, *S. henryense*, *S. imbricatum*, *S. incommmodum*, *S. inundatum*, *S. itatiaiae*, *S. jensenii*, *S. junghuhnianum*, *S. kenaiense*, *S.*

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hasianum, *S. laegaardii*, *S. lapazense*, *S. laxirameum*, *S. lenense*, *S. leonii*, *S. lescurii*, *S. lewisii*, *S. liesneri*, *S. limbatum*, *S. lindbergii*, *S. longicomosum*, *S. macrophyllum*, *S. magellanicum*, *S. majus*, *S. mendocinum*, *S. meridense*, *S. microcarpum*, *S. microporum*, *S. molle*, *S. monzonense*, *S. nemoreum*, *S. noryungasense*, *S. novo-zelandicum*, *S. obtusum*, *S. olafii*, *S. orientale*, *S. ovatum*, *S. oxyphyllum*, *S. pacificum*, *S. palustre*, *S. papillosum*, *S. patens*, *S. perfoliatum*, *S. perichaetiale*, *S. planifolium*, *S. platyphylloides*, *S. platyphyllum*, *S. portoricense*, *S. priceae*, *S. pseudoramulinum*, *S. pulchricoma*, *S. pulchrum*, *S. pulvinatum*, *S. pycnocladulum*, *S. pycnocladum*, *S. pylaesii*, *S. quinquefarium*, *S. reclinatum*, *S. recurvum*, *S. riparium*, *S. ripense*, *S. rotundatum*, *S. rubellum*, *S. rubiginosum*, *S. rubroflexuosum*, *S. russowii*, *S. sancto-josephense*, *S. santanderense*, *S. schofieldii*, *S. sericeum*, *S. sjorsii*, *S. skyense*, *S. slooveri*, *S. sonsonense*, *S. sparsum*, *S. squarrosus*, *S. steerei*, *S. strictum*, *S. subditivum*, *S. subfulvum*, *S. subhomophyllum*, *S. subnitens*, *S. subobesum*, *S. subsecundum*, *S. subtile*, *S. sucrei*, *S. tenellum*, *S. tenerum*, *S. teres*, *S. torreyanum*, *S. triporosum*, *S. trirameum*, *S. troendelagicum*, *S. truncatum*, *S. tundrae*, *S. uleanum*, *S. viride*, *S. vitjianum*, *S. warnstorffii*, *S. wheeleri*, *S. wilfii*, and *S. wulfianum*). Thus, transformation of mosses and liverworts is not taught within the full scope of the claims.

Furthermore, the specification must teach how to carry out the invention, and it does not teach how to transform *C. purpureus* or *M. polymorpha*. See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

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Dr. Gorr urges that of 5 *Physcomitrella* species, only *P. patens* has been transferred to axenic *Physcomitrella patens* culture, but one of skill in the art would not expect other *Physcomitrella* species to behave differently (§5-6).

This is not found persuasive because more than culturing is required.

Dr. Gorr urges that protoplasts have been isolated from *C. purpureus*, *F. hygrometrica*, and *M. polymorpha* and one of ordinary skill in the art would be able to adapt protoplast protocols for other bryophytes (§9-10).

This is not found persuasive because establishing these methods within the full scope of the claims would be beyond one of ordinary skill in the art.

Dr. Gorr urges that transformation protocols are known for *P. patens*, *C. purpureus* and *M. polymorpha* and one of ordinary skill in the art would be able to adapt transformation protocols for other bryophytes, citing his use of the Reuter protocol on *F. hygrometrica* and *M. polymorpha* and that these excrete proteins (§11-18 and 21-23).

This is not found persuasive. Transformation of these species is not taught in the specification. Furthermore, these species do not represent the full scope of the claims.

Dr. Gorr urges that Zeidler and Nasu teach that methods have been developed for culturing *C. purpureus* and *M. polymorpha*, he himself cultured *C. purpureus*, *F. hygrometrica*, *Pylaisus selwynii*, *Pylaisia polyantha*, *Jungermania leiantha* and *M. polymorpha*, and one of ordinary skill in the art would be able to develop culture protocols for other bryophytes (§7-8, 19-20).

This is not found persuasive because more than culturing is required. It is also noted that Dr. Gorr is one of extraordinary skill in the art.

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Applicant urges that the specification describes species of moss and liverwort suitable for practicing the instant invention, citing Reski and Rudolph, and methods of transformation of *P. patens* (response pg 13-14).

This is not found persuasive. Reski only discusses transformation of *P. patens*, and Rudolph only discusses growth of Sphagnum in culture, not transformation. Transformation of *P. patens* does not teach transformation of mosses and liverworts within the full scope of the claims.

Applicant urges that a working example is present (response pg 15).

This is not found persuasive because the working example does not teach species within the full scope of the claims.

Applicant urges that the organisms used in the method have been well-characterized, and are simple and predictable, citing Reski, Houba-Herin, Reutter, Zeidler, Nasu, Rasmussen, and Muhlbach (response pg 15-16).

This is not found persuasive. The majority of these articles only discuss *P. patens*, including Muhlbach, and none teach transformation of mosses and liverworts within the full scope of the claims.

Applicant urges that the skill of those in the art is very high, citing the inventor Dr. Gorr (response pg 16).

This is not found persuasive. Dr. Gorr is one of extraordinary skill in the art.

Applicant urges that Ceradon and Marchantia have been transformed; indicating transformation of protonema-producing plants is predictable (response pg 17).

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This is not found persuasive because only *P. patens*, *C. purpureus* and *M. polymorpha* have been transformed. These are not a representative sample of the 20,000 bryophytes cited by Dr. Gorr in his Declaration.

See *In re Vaeck* (CAFC 1991) 20 USPQ2d 1438 at pg 1445:

In so doing we do not imply that patent applicants in art areas currently denominated as "unpredictable" must never be allowed generic claims encompassing more than the particular species disclosed in their specification. It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re Angstadt*, 537 F.2d 498, 502-03, 190 USPQ 214, 218 (CCPA 1976). However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility.

Applicant urges that while some experimentation may be necessary, it would not be undue (response pg 17-18).

This is not found persuasive because transformation procedures would need to be worked out for a broad range of mosses and liverworts.

Applicant urges that protonema has a defined meaning, and the method claims two steps; thus claim 1 is not overly broad (response pg).

This is not found persuasive because practicing the inventions requires transformation of a broad range of mosses and liverworts, which is not taught by the specification. Thus, claim 1 is very broad.

Applicant urges that multiple species of mosses and liverworts have been transformed and Dr Gorr shows it is easy to transform others (response pg 19).

This is not found persuasive because transformation of 1 species in the specification, two in the prior art, and one in the Declaration is not a representative sample of the 20,000 bryophyte species encompassed by the claims.

Claim Rejections - 35 USC § 103

5. Claims 1-5 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Houba-Hérin et al (1999, Plant J. 17:615-626) in view of Reutter et al (1996, Plant Tiss. Cult. Biotechnol. 2:142-147). The rejection is modified from the rejection set forth in the Office action mailed 7 June 2005, as applied to claims 1-5 and 7-13. Applicant's arguments and the Declaration of Dr. Gorr, both filed 7 December 2005 have been fully considered but they are not persuasive.

The claims are drawn to a method of isolating a heterologous protein from culture medium in which in *P. patens* protonema were grown.

Houba-Hérin et al teach a method of producing a biologically active heterologous protein in the moss *P. patens*. The protein was a maize cytokinin oxidase and the activity of this enzyme was detected in the culture medium in which protoplasts were grown (pg 619, right column, paragraph 1). Houba-Hérin et al do not disclose isolation of the enzyme in culture media in which protonema were grown.

Reutter et al teach growth of *P. patens* protonema transformed with a nucleic acid encoding a heterologous protein (pg 143, paragraph 2-3) and that these protonema produced large amounts of the heterologous protein (Fig. 3). Reutter et al also teach that *P. patens* can be grown on inorganic medium (pg 142, paragraph 4).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing a heterologous protein in *P. patens* as taught by Houba-Hérin et al, to grow the protoplasts to the protonema stage as described in Reutter et al. One of ordinary skill in the art would have been motivated to do so because Houba-Hérin et al

suggest producing the enzyme in a moss system in order to get the proper processing of the enzyme (pg 621, right column, paragraph 2).

Dr. Gorr urges that Houba-Hérin et al merely teaches transient transformation in order to prove the functionality of an enzyme; it does not related to the production of heterologous substances and heterologous DNA is not integrated into the genome (§24).

This is not found persuasive. The methods steps practiced by Houba-Hérin et al in view of Reutter et al are identical to the method steps of the claimed methoda and heterologous substances are produced. Integration of heterologous DNA into the genome is a limitation not included in the claims.

Dr. Gorr urges that Houba-Hérin et al selected transformed protoplasts because the glycosylated form may be kept in the cell wall and the unglycosylated form in an internal compartment (§24).

This is not found persuasive. This is not what Houba-Hérin et al say at all. Houba-Hérin et al are discussing the possibility that corn may have more than one gene encoding CKO, one of which does not produce a glycosylated protein.

Dr. Gorr urges Houba-Hérin et al used protoplasts not cell-wall containing tissue; at 44 hr after transformation cells walls would not have formed (§24-25).

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Dr. Gorr urges Houba-Hérin et al do not provide motivation to do the instant method (¶26).

This is not found persuasive because Houba-Hérin et al suggest producing the enzyme in a moss system in order to get the proper processing of the enzyme; this would require secretion (pg 621, right column, paragraph 2).

Dr. Gorr urges in Reutter no heterologous protein was excreted into the medium, and such excretion is not suggested (¶28).

This is not found persuasive. Applicant is again arguing against the references individually; one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references.

Dr. Gorr urges one of ordinary skill in the art would derive to motivation to combine the references and even if they did, the combination would not teach or suggest there would be secretion of the heterologous protein through the cell wall (¶28).

This is not found persuasive. Motivation is provided and applicant's error in interpretation of what Houba-Hérin et al meant when discussing the cell wall is discussed above.

Applicant urges that Houba-Hérin et al teach transforming protoplasts, not transformed protonema tissue, producing cells without cell walls, that the process of transforming protoplasts is not an element of the claimed invention, and that one of skill in the art could not have predicted that protonema would be a good approach because protonema have cell walls (response pg 20-22).

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the

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rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Furthermore, producing secreted proteins in cell wall containing organisms is well-known in the art; see, for example, Dorsey (1998, US Patent 5,776,730); Radin et al (1999, US Patent 5,929,304, see column 31, lines 30-52).

Applicant urges that Reutter is silent with respect to obtaining GUS produced by the protonema without disrupting tissues; they had to lyse the tissues (response pg 22-23).

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant urges that the references do not teach how such protocols could be combined and provide no motivation for the combination (response pg 26).

This is not found persuasive. Houba-Hérin et al suggest producing the enzyme in a moss system in order to get the proper processing of the enzyme (pg 621, right column, paragraph 2).

6. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Houba-Hérin et al in view of Reutter et al as applied to claims 1-2, 4-5 and 17-18 above, and further in view of Nasu et al (1997, J. Ferm. Bioengin. 84:519-523). The rejection is modified from the rejection set forth in the Office action mailed 7 June 2005. Applicant's arguments and the Declaration of Dr. Gorr, both filed 7 December 2005 have been fully considered but they are not persuasive.

The claims are drawn to a method of isolating a heterologous protein from culture medium in which in liverwort protonema were grown.

The teachings of Houba-Hérin et al in view of Reutter et al are discussed above. Houba-Hérin et al in view of Reutter et al do not disclose a method of isolating a heterologous protein from culture medium in which in protonema were grown, wherein the protonema were from a liverwort.

Nasu et al teach transformation of *Marchantia polymorpha* (pg 520, left column, paragraphs 1-2). *M. polymorpha* is a photoauxotroph, and thus its growth does not require sugars, vitamins, or phytohormones.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing a heterologous protein in protonema tissue as taught by Houba-Hérin et al in view of Reutter et al, to use liverwort protonema as described in Nasu et al. One of ordinary skill in the art would have been motivated to do so because substitution of one bryophyte for another is an obvious optimization of design parameters.

Dr. Gorr urges that Nasu does not teach or suggest there would be secretion of heterologous protein through cell walls (¶28).

This is not found persuasive. Applicant's error in interpretation of what Houba-Hérin et al meant when discussing the cell wall is discussed above.

Applicant urges that Nasu teaches a method of transformation of *M. polymorpha*, and not cultures of intact plant tissue (response pg 24-25).

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

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Applicant urges that the references do not teach how such protocols could be combined and provide no motivation for the combination (response pg 26).

This is not found persuasive. Houba-Hérin et al suggest producing the enzyme in a moss system in order to get the proper processing of the enzyme (pg 621, right column, paragraph 2).

7. Claims 1-5 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reutter et al (1996, Plant Tiss. Cult. Biotechnol. 2:142-147) in view of Raskin (2000, US Patent 6,096,546, filed 1998).

The claims are drawn to a method of isolating a heterologous protein from culture medium in which in protonema were grown.

Reutter et al teach growth of *P. patens* protonema transformed with a nucleic acid encoding a heterologous protein (pg 143, paragraph 2-3) and that these protonema produced large amounts of the heterologous protein (Fig. 3). Reutter et al also teach that *P. patens* can be grown on inorganic medium (pg 142, paragraph 4). Reutter et al do not disclose isolation of heterologous protein from in the media.

Raskin teaches isolation of heterologous proteins from in the media in which transformed plants are grown (column 9, line 19, to column 12, line 67)

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing a heterologous protein from protonema as taught by Reutter et al, to secrete the protein into the media as described in Raskin. One of ordinary skill in the art would have been motivated to do so because of the advantages of isolating of the protein without disrupting the cells (Raskin, column 30, lines 30-67)

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne Kubelik, Ph.D.
March 6, 2006



ANNE KUBELIK, PH.D.
PRIMARY EXAMINER